



**ORAL PRESENTATION**

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# Multiparametric cardiovascular magnetic resonance assessment of cardiac allograft vasculopathy

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## Background

Cardiac allograft vasculopathy (CAV) continues to limit the long-term survival of heart transplant recipients. CAV affects both the epicardial arteries and the microvessels, however it does so independently, and epicardial and microvascular disease are both independently predictive of prognosis. Despite being associated with considerable limitations, coronary angiography has a class I recommendation for CAV surveillance and annual or biannual surveillance angiography is performed routinely in most centers. The aim of this study was to evaluate the diagnostic performance of multiparametric CMR in CAV, and to compare the performance of CMR to that of invasive coronary angiography, using contemporary invasive epicardial artery and microvascular assessment techniques as reference standards.

## Methods

All transplant recipients referred for surveillance angiography at a single UK transplant center over a 2-year period were prospectively screened for study eligibility. Patients prospectively underwent coronary angiography followed by coronary intravascular ultrasound (IVUS; epicardial artery reference standard) and index of microcirculatory resistance (IMR; microvascular reference standard). Within one month patients underwent multiparametric CMR. CMR assessment included LV volumetrics, circumferential strain and strain rate, torsion (circumferential-longitudinal shear), pixel-wise absolute myocardial blood

flow quantification using generalized Tikhonov deconvolution with a b-spline representation of the impulse response function, late gadolinium enhancement and T1 mapping/extracellular volume measurement. Angiographic and CMR data were compared with the invasive epicardial artery (IVUS intima-media ("plaque") volume index) and microvascular (IMR) reference standards. In addition, 10 age- and sex-matched healthy volunteers underwent CMR.

## Results

Forty-eight patients were recruited; median 7.1 years (IQR 4.6-10.3) since transplantation. Mean IVUS plaque volume index was  $22.4 \pm 9.8\%$ ; mean IMR was  $23.7 \pm 12.5$ . Selected univariable and multivariable associations between patient, angiographic and CMR data and IVUS plaque volume index and IMR are summarized in Table 1. CMR myocardial perfusion reserve was the only independent predictor of both epicardial ( $\beta = -0.57$ ,  $p < 0.001$ ) and microvascular disease ( $\beta = -0.60$ ,  $p < 0.001$ ) on stepwise multivariable regression. Myocardial perfusion reserve outperformed angiography for detecting moderate CAV (AUC 0.89, 95% confidence intervals 0.79-1.0 v 0.59 (0.42-0.77) respectively,  $p = 0.01$ ; Figure 1A) and severe CAV (AUC 0.88 (0.78-0.98) v 0.67 (0.52-0.82),  $p = 0.05$ ; Figure 1B).

## Conclusions

CAV, including epicardial and microvascular components, can be detected more accurately using non-invasive CMR-based absolute myocardial blood flow assessment than with invasive coronary angiography, the current clinical surveillance technique.

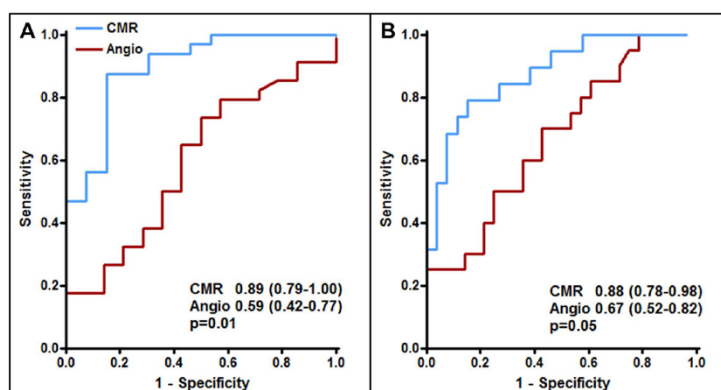
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**Table 1 Associations between patient characteristics, angiography data and CMR data with invasive reference standards of epicardial artery disease (IVUS plaque volumes index; 1) and microvascular disease (IMR; 2).**

| 1. Associations with coronary intravascular ultrasound (IVUS) plaque volume index |  |         |         |
|---|--|---------|---------|
| Univariable associations  | A. Patient characteristics                                 | $\beta$ | p value |
|   | Time since transplantation                                 | 0.49    | 0.001   |
|   | Donor age  | 0.29    | 0.058   |
|   | B. Angiography data  |         |         |
|   | Maximum angiographic stenosis                              | 0.33    | 0.024   |
|   | C. CMR data  |         |         |
|   | Early diastolic SR   | -0.38   | 0.014   |
|   | MPR  | -0.55   | < 0.001 |
|   | Infarct LGE  | 0.35    | 0.022   |
| Multivariable stepwise regression   | A. Including patient characteristics and angiographic data |         |         |
|   | Time since transplantation                                 | 0.49    | 0.001   |
|   | B. Including patient characteristics and CMR data          |         |         |
|   | Time since transplantation                                 | 0.47    | < 0.001 |
|   | Early diastolic SR   | -0.24   | 0.049   |
|   | MPR  | -0.57   | < 0.001 |
| 2. Associations with index of microcirculatory resistance (IMR)                   |  |         |         |
| Univariable associations  | A. Patient characteristics                                 |         |         |
|   | Donor age  | 0.39    | 0.007   |
|   | Donor hypertension   | 0.35    | 0.016   |
|   | B. Angiography data  |         |         |
|   | Maximum angiographic stenosis                              | -0.16   | 0.281   |
|   | C. CMR data  |         |         |
|   | LVEF   | -0.36   | 0.015   |
|   | $\epsilon$ cc  | 0.46    | 0.002   |
|   | MPR  | -0.55   | < 0.001 |
| Multivariable stepwise regression   | Donor hypertension   | 0.29    | 0.012   |
|   | EF   | -0.26   | 0.024   |
|   | MPR  | -0.60   | < 0.001 |

Only selected data is shown due to table size constraints. 1. On univariable analysis, maximum angiographic stenosis showed a significant association with plaque volume index, however after correcting for time since transplantation, this relationship was no longer significant. Early diastolic strain rate (SR), myocardial perfusion reserve (MPR) and infarct late gadolinium enhancement (LGE) were significantly associated with plaque volume index on univariable analyses, but only MPR and early diastolic SR remained independently associated with plaque volume index on multivariable analysis. 2. Maximum angiographic stenosis was not significantly associated with IMR on univariable analysis. Patient characteristics including donor age and donor hypertension showed significant associations with IMR on univariable analyses, as did CMR parameters such as LV ejection fraction (EF), peak systolic circumferential strain ( $\epsilon$ cc) and MPR. On multivariable analysis only donor hypertension, EF and MPR remained independently associated with IMR.



**Figure 1 Diagnostic performance of cardiovascular magnetic resonance myocardial perfusion reserve and angiography for detecting cardiac allograft vasculopathy (CAV).** Diagnostic performance of cardiovascular magnetic resonance myocardial perfusion reserve (CMR) and angiography (angio) for detecting; (A) moderate cardiac allograft vasculopathy, defined as > median epicardial or microvascular disease; and (B) severe cardiac allograft vasculopathy, defined as > 75th centile epicardial or microvascular disease.

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